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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/845,938	04/30/2001	Alexander V. Kabanov	3874-129 US	3307

26817 7590 09/22/2004

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EXAMINER	
LI, QIAN JANICE	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 09/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/845,938	KABANOV ET AL.	
	Examiner	Art Unit	
	Q. Janice Li	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 June 2004* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *29-40 and 70-77* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *29-40 and 70-77* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The response and amendment filed 6/25/04 have been entered. Claims 29-35, 37, 38, 40, 70-72, and 77 have been amended. Claims 29-40 and 70-77 are pending and under current examination.

Unless otherwise indicated, previous rejections that have been rendered moot in view of the amendment to pending claims will not be reiterated. The arguments in 6/25/04 response would be addressed to the extent that they apply to current rejection.

Priority

Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. § 120 as follows:

The newly submitted benefit of priority claim does not comply with the requirement set forth in 37 CFR 1.78(a)(2) and (a)(5), because the specific reference to any prior nonprovisional application must be submitted during the pendency of the application, and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application. This time period is not extendable (37 CFR § 1.78 (2) ii). If the reference required by 35 U.S.C. 120 and paragraph (a)(2) of this section is resented in a nonprovisional application after the time period provided by paragraph (a)(2) of this section, the claim under 35 U.S.C. 120, 121, or 365(c) for the benefit of a prior filed copending nonprovisional application or international application designating the United States of America may be accepted if

the reference identifying the prior application by application number or international application number and international filing date was unintentionally delayed. A petition to accept an unintentionally delayed claim under 35 U.S.C. 120, 121, or 365(c) for the benefit of a prior filed application must be filed as required by 37 CFR § 1.78 a (3).

Assuming the applicants will file the petition which presumed to be granted subsequently, the later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application); the disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994). In the instant case, the subject matter concerning activation of dendritic cells and modulation of immune response was not present until the filing of the U.S. provisional application 60/200,487, filed April 28, 2000. Thus, the priority date for the subject matter has been established as the filing date of the provisional application.

Specification

The specification is objected to because it contains sequence disclosures (page 49, line 27) that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2) but are not identified in the specification by sequence identifier numbers. Applicant must provide sequence identifiers, in the case that these sequences are not included in the original sequence

submission, a paper copy and a computer readable copy of the Sequence Listing and a statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 CFR 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d). A full response to this Office Action must include a complete response to the requirement for a Sequence Listing.

Further the lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors in sequence compliance. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 29-40 and 70-77 stand rejected under 35 U.S.C. 112, first paragraph, for reasons of record in the paragraph bridging pages 7 and 8 of the Office action mailed 3/23/04. Applicants fail to respond to the issue raised, and thus the rejection stands.

Particularly, the specification fails to teach that the block copolymer could increase the immune response induced by a *viral* vector polynucleotide, thus fails to support the full scope of the claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.
>
> (f) he did not himself invent the subject matter sought to be patented.

Claims 29-40 and 70-77 stand rejected under 35 U.S.C. 102(e) as being anticipated by *Manthorpe et al* (US 2002/0,019,358).

Manthorpe et al teach a method comprising administering to a mammal a composition comprising a polynucleotide and an auxiliary agent that is a non-ionic polyoxyethylene-polyoxypropylene block copolymer comprises at least Pluronic F127 and L61 (claims 1, 28, 29, 38-40, and table V), wherein the composition could be administered via various routes such as intramuscular and subcutaneous routes (paragraph 0136) for inducing a desired immune response (claim 40), wherein the polynucleotide could encode an antigen and a cytokine (e.g. paragraph 0120), wherein the cytokine could be GM-CSF or IL-12 (e.g. paragraph 0135), wherein the polynucleotide comprises a promoter such as CMV (e.g. figure 1 and paragraph 0029). Accordingly, *Manthorpe et al* anticipate the instant claims.

Applicants argue that the cited publication is drawn to the use of salts and auxiliary agents, and does not contemplate a polynucleotide encodes an adjuvant.

In response, as indicated above, the cited patent does teach a polynucleotide encoding an antigen and a cytokine (adjuvant), and the block copolymer as auxiliary agent in the composition, thus the disclosed composition meet instant claim limitation.

The prior rejection of Claims 29-40 and 70-77 under 35 U.S.C. 102(e) as being anticipated by *Kabanov et al* (US 6,387,406), is withdrawn because Kabanov et al fail to teach a polynucleotide encoding an antigen and an adjuvant.

The prior rejection of Claims 29-40 and 70-77 rejected under 35 U.S.C. 102(e) as being anticipated by *Kabanov et al* (US 6,656,459), is withdrawn because Kabanov et al fail to teach a polynucleotide encoding an antigen and an adjuvant.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The prior rejection of Claims 29, 31, 32, 34, 36, 37, 39, 40, 70, 72, 74-77 under 35 U.S.C. 103(a) as being unpatentable over *Raz et al* (US 6,589,940), in view of *Kabanov et al* (5,656,611, IDS), and evidenced by *Jakob et al* (J Immunol 1998;161:3042-9), is withdrawn because Raz et al do not teach a polynucleotide encoding an antigen and a cytokine.

Claims 29, 31, 32, 34, 36, 37, 39, 40, 70, 72, 74-77 stand rejected under 35 U.S.C. 103(a) as being unpatentable over *Carson et al* (US 5,830,877), in view of *Kabanov et al* (5,656,611).

Carson et al teach a method for inducing immune response to an antigen comprising delivering a polynucleotide encoding the antigen and an immunostimulatory peptide to a host cell (e.g. abstract and column 7, lines 29-45) by intradermal or intramuscular injection of the polynucleotide, wherein the immunostimulatory peptide is a cytokine (e.g. claim 15) and served as an adjuvant for the vaccine antigen (column 8, lines 41-53), wherein the polynucleotide could be driven by a CMV promoter (column 15, lines 45-63). *Carson et al* also teach using cationic liposome to enhance gene delivery (column 3, lines 24-25) as well as using detergent known in the art to facilitate transfection of the polynucleotide (e.g. column 6, lines 11-14, and column 11, lines 3-5). They go on to teach that the Th1 response induced by the polynucleotide is the result of antigen activation of antigen-presenting cells such as dendritic cells (column 7, § t.). *Carson et al* clearly suggested the use of detergent to facilitate the transfection and

referred to it as art known knowledge, but do not specifically teach the polyoxyethylene-polyoxypropylene block copolymer or the state of the block copolymer.

Kabanov et al supplemented the teaching of *Carson et al* by establishing that it is well known in the art that block copolymer as a type of detergent could increase the stability of a polynucleotide and increase the ability of nucleic acids to cross cell membranes and acting in the interior of a cell (abstract). *Kabanov et al* particularly teach the polyoxyethylene-polyoxypropylene block copolymer (e.g. columns 7 and 8), the state of the copolymer, and how to avoid gel formation of the composition (column 11).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the methods taught by *Carson et al* by simply using the copolymer as taught by *Kabanov et al* in the method of *Carson et al* with a reasonable expectation of success. The ordinary skilled artisan would have been motivated to modify the claimed invention because the copolymer could enhance the cell entry, thus, the efficacy of the polynucleotide. Thus, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Claims 29, 31, 32, 34, 36, 37, 39, 40, 70, 72, 74-77 are rejected under 35 U.S.C. 103(a) as being unpatentable over *Mathiowitz et al* (US 6,677,313), in view of *Kabanov et al* (5,656,611).

Mathiowitz et al teach a method for inducing immune response to an antigen comprising delivering a polynucleotide encoding an antigen and a cytokine to a host cell (e.g. abstract and column 18, lines 50-54), wherein mucosal route is preferred because

it is rich in immune system cells, wherein the polynucleotide could be driven by a CMV promoter (e.g. fig. 1). *Mathiowitz et al* also teach using copolymers to enhance gene delivery, provide extensive list of polymers as non-limiting embodiment and the state of formulation (columns 7-12). Although *Mathiowitz et al* did not particularly mention dendritic cells, the teaching of delivering the polynucleotide to immune cell-rich mucosa coupled with the agents delivered (antigen and cytokine) would have suggested to the ordinary skilled artisan as stimulating/activating dendritic cells because it is well known in the art that mucosal and epidermal are dendritic cell-rich tissue, dendritic cells are antigen processing/presenting cells, and it is well known in the art upon contacting antigens, dendritic cells would be activated. *Mathiowitz et al* do not specifically teach the polyoxyethylene-polyoxypropylene block copolymer.

Kabanov et al supplemented the teaching of *Mathiowitz et al* by establishing that it is well known in the art that the polyoxyethylene-polyoxypropylene block copolymer is a type of polymer that could increase the stability of a polynucleotide and increase the ability of nucleic acids to cross cell membranes and acting in the interior of a cell (abstract). *Kabanov et al* particularly teach the polyoxyethylene-polyoxypropylene block copolymer (e.g. columns 7 and 8), the state of the copolymer, and how to avoid gel formation of the composition (column 11).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the methods taught by *Mathiowitz et al* by simply using the copolymer as taught by *Kabanov et al* in the method of *Mathiowitz et al* with a reasonable expectation of success. The ordinary skilled artisan would have been

motivated to modify the claimed invention because the copolymer could enhance the cell entry, thus the efficacy of the polynucleotide, which would lead to activation of dendritic cells if the polynucleotide expresses agents that are capable of stimulating/activating dendritic cells. Thus, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Claims 30, 33, 35, 38, 71, and 73 stand rejected under 35 U.S.C. 103(a) as being unpatentable over *Carson et al* (US 5,830,877) or *Mathiowitz et al* (US 6,677,313), and *Kabanov et al* (5,656,611) as applied to claims 29, 31, 32, 34, 36, 37, 39, 40, 70, 72, and 74-77 above, further in view of *Alakhov et al* (6,218,438) or *Kabanov et al* (6,387,406), or *Manthorpe et al* (US 2002/0,019,358).

The combined teachings of *Carson et al or Mathiowitz et al* and *Kabanov et al* do not particularly disclose a block copolymer comprising at least Pluronic F127 and L61. However, before the effective filing date of the instant invention, *Alakhov et al* teach that the block copolymers could be formulated with a biological agent comprising Pluronic F127 and L61 (Tabs 5 & 9), the teaching of *Kabanov et al* and *Manthorpe et al* also established that it is well known in the art that block polymers comprising Pluronic F127 and L61 are effective adjuvant for polynucleotide delivery.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the methods taught by *Carson et al and Kabanov et al* by simply using the specific Pluronic F127 and L61 copolymer as taught by *Alakhov et al Kabanov et al* or *Manthorpe et al* in the method of *Carson et al or*

Mathiowitz with a reasonable expectation of success. The ordinary skilled artisan would have been motivated to modify the claimed invention because it is within the bound of optimization of a copolymer formulation. Thus, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 29-40 and 70-77 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 2, 3, 13, 18, 21, and 23 of U.S. Patent No. 6,359,054.

Although the claims of the cited patent do not recite specifically the antigen and cytokine, these are taught in the text of the specification. Accordingly, the claimed processes in the cited patent and the present application are obvious variants. Inventions as claimed are co-extensive.

Applicants request to defer resolution of this rejection until a later time and acknowledged the willingness to file a terminal disclaimer if necessary.

Until then, for reasons of record and set forth above, the rejection stands.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Q. Janice Li** whose telephone number is 571-272-0730. The examiner can normally be reached on 9:30 am - 7 p.m., Monday through Friday, except every other Wednesday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Amy Nelson** can be reached on 571-272-0804. The fax numbers for the organization where this application or proceeding is assigned are **703-872-9306**.

Any inquiry of formal matters can be directed to the patent analyst, **Dianiece Jacobs**, whose telephone number is (571) 272-0532.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Q. Janice Li
Primary Examiner
Art Unit 1632

QJL
September 17, 2004